UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,596	12/07/2001	Michael M. Becker	GP123-02.UT	6565

21365 7590 11/26/2004

GEN PROBE INCORPORATED
10210 GENETIC CENTER DRIVE
SAN DIEGO, CA 92121

EXAMINER	
SISSON, BRADLEY L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,596	BECKER, MICHAEL M.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25,27-32,34-36 and 61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25,27-32,34-36 and 61* is/are rejected.

7)☒ Claim(s) *36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states that various documents have been incorporated by reference. Such omnibus language fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited documents. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

> Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USQP 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Attention is also directed to MPEP 608.01(p)I, which, in pertinent part, is reproduced below:

> Mere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph. In re de Seversky, 474 F.2d 671, 177 USPQ 144 (CCPA 1973). In addition to other requirements for an application, the referencing application should include an identification of the referenced patent, application, or publication. Particular attention should be directed to specific portions of

the referenced document where the subject matter being incorporated may be found. (Emphasis added)

Accordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in part or in whole, the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

Response to traversal

2. Acknowledgement is made of applicant having deleted the paragraph entitled "Incorporation by Reference," and the amendments to paragraphs found at page 4-8, 10-12, 16, 20, 21, 23-24, 27, 35-38, and 40. The mere referencing that the cited documents are to be considered to be incorporated by reference does not teach why the various documents are to be incorporated, nor does it direct one to the relevant portion(s) of the various documents. Accordingly, and in the absence of convincing evidence to the contrary, the documents have, for purposes of examination, not been considered to be incorporated by reference and as such, he specification remains objected to.

3. The disclosure is objected to because of the following informalities:

4. The amendment filed 26 August 2004 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

a. The insertion of language throughout the specification that various documents have been incorporated by reference.

b. The deletion of text referencing foreign applications with those identifying US Patent applications.

c. The amendment to page 4 where the adjective "positive" was replaced with "negative" in describing the "net charge" of a polynucleotide that is bound to cationic groups. It is noted that the cationic nature of the polynucleotide is the result of the polynucleotide having been linked to a cation. While applicant's representative asserts that this is an obvious mistake, and in support of such a position directs attention to page 29, last paragraph, bridging to page 30 of the specification, a review of the cited passage fails to clarify the issue. As noted in the sentence that spans pages 29 and 30, the polynucleotides are attracted to and bind to polycations. It is this compound of polynucleotides and (poly)cations that are considered to be referenced at page 4 of the disclosure, not naked polynucleotides.

d. Applicant is required to cancel the new matter in the reply to this Office Action.

5. Appropriate correction is required.

Claim Objections

6. Claim 36 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 36 fails to limit claim 33, the claim from which it depends, as claim 33 has been canceled.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-25, 27-32, 34-36, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

9. For convenience, claim 1, the sole independent claim under consideration, is reproduced below.

1. (Currently Amended) A method for ~~forming a duplex from a polynucleotide probe and~~ determining the presence of a target nucleic acid in a sample, said method comprising: ~~providing the following to a test sample:~~

a) providing to a sample a negatively charged polynucleotide probe and a synthetic, water soluble polycationic polymer, wherein said probe is provided to said sample under conditions permitting said probe to preferentially hybridize to a target nucleic acid, ~~if present,~~ which may be present in said sample, thereby forming a probe:target duplex, and wherein said ~~a synthetic polycationic~~ polymer is provided to said sample in an amount sufficient to increase the association rate of said probe and said target nucleic acid in said sample under said conditions; ~~and~~

b) exposing said sample to a dissociating reagent in an amount sufficient to dissociate said polymer from said ~~probe and said target nucleic acid~~ duplex after said probe and said target nucleic acid have had sufficient time to associate in said sample; and

c) determining whether said duplex is present in said sample as an indication of the presence or absence of said target nucleic acid.

10. For purpose of examination, claim 1 has been construed as encompassing the simultaneous detection of an infinite number of target nucleic acids, that the target nucleic acids can have different rates of annealing with a complementary sequence, and that conditions under which polycationic polymer dissociation may occur for one target/probe duplex can be the same conditions under which a different target/probe duplex would also dissociate, thereby proscribing the detection of other targets nucleic acids present in the mixture and which artisan is attempting to detect.

11. A review of the disclosure finds but two examples; Example 1, pages 42-48, and Example 2, page 49. As seen in Example 1, six different polymers were tested:

- poly-L-lysine hydrobromide with a molecular weight of from 20,000 to 30,000 Da
- poly-L-lysine hydrobromide with a molecular weight of from 150,000 to 300,000 Da
- poly (lys, tyr) 4:1, with an indicted molecular weight of 24,600 Da (visible)

- poly-L-histidine hydrochloride with an indicted molecular weight of 15,800 Da (using low angle laser light scattering)
- poly-L-arginine hydrochloride with an indicated molecular weight of 11,800 (visible)
- Hexadimethrine bromide

12. None of the examples teach the use of any cation, be it poly' or otherwise, other than the oligopeptides described above. Furthermore, the specification fails to teach the detection of one nucleic acid over that of another, highly related sequence, e.g., a sequence that has a single point mutation. Also, the specification fails to teach how the claimed method is to be practiced when a virtually infinite number of polynucleotides are to be detected in a simultaneous manner when no label is used.

13. As presently worded, the reactants only need to be exposed to a "dissociation reagent in an amount sufficient to dissociate said polymer from said duplex." For purposes of examination, the "dissociation reagent" ha been construed as encompassing the hybridization buffer, water, or any other reactant that, when heated to various conditions, would result in said dissociation. It is further noted that while the claims stipulate that there needs to be a sufficient "amount," it does not have to be under conditions that would result in said dissociation, nor does the claim require that any dissociation actually take place.

It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43

USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

For the above reasons, an in the absence of convincing evidence to he contrary, claims 1-25, 27-32, 34-36, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

14. Claims 1-25, 27-32, 34-36, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth

> as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

15. For purposes of examination, the method of claim 1 has been construed as encompassing the detection of any number of different target polynucleotides with any one or more probes in a simultaneous manner where no label or detection means is employed. Said method ahs also been construed as encompassing performing all method steps with the reactants in solution and no apparent means for retaining duplex should one reactant be removed from the solution.

16. For purposes of examination, the phrase "forming a duplex" has been interpreted as encompassing forming both duplex and triplex structures, as a triplex structure comprises a duplex structure. The clause "in an amount sufficient to increase the association rate of said probe an said target nucleic acid" has been interpreted as encompassing values that both allow for an exceed this increased rate of association.

17. The term "polycationic polymer" has been interpreted as fairly encompassing both organic and inorganic polycationic polymers, where said polymers can exhibit the range of hydrophobicity and hydrophilicity and can have virtually any upper mass (claim 7 excepted).

18. While claim 1 has been limited in that the conditions used are such that it the probe will "preferentially hybridize" to the target, such language has been interpreted as fairly encompassing the formation of duplex structures with non-target sequences in nearly equal amounts.

19. As presented above, the specification provides two examples, neither of which fully enables the claimed invention.

20. As presented above, the specification fails to provide a written description of the invention in such full, clear, and concise language so as to reasonably suggest that applicant had possession of the invention at the time of filing. With the record not establishing that applicant had possession of the invention, and recognizing that one cannot enable that which they do not yet possess, claims 1-25, 27-32, 34-36, and 61 are deemed non-enabled by the instant disclosure. While applicant has amended the specification so to indicate that various documents are incorporated by reference, said document, as noted above, are improperly incorporated by reference and as such, applicant cannot now rely upon said disclosures in an attempt to fulfill the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

21. Therefore, and in the absence of convincing evidence to the contrary, claims 1-25, 27-32, 34-36, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Response to argument

22. At page 25 of the response received 26 August 2004, hereinafter the response, applicant asserts that issues of enablement have been overcome by applicant's incorporation by reference of documents in the disclosure. This argument ahs been fully considered and has not been found persuasive or reasons of record, *supra*.

23. At page 25 of the response applicant's representatives provides conclusory remarks as to what the level of skill is in the art, and what aid skilled artisan would have been capable of accomplishing without resorting to undue experimentation.

24. This argument has been fully considered and has not been found persuasive. Attention is directed to MPEP 2145.

> Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art.
> The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration.

25. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-25, 27-32, 34-36, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

26. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

27. Claims 1-25, 27-32, 34-36, and 61 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 1-25, 27-32, 34-36, and 61 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the specification at page 1, "Field of the Invention," and in original claim 1. In both instance applicant has stated that the invention relates to a method of forming duplexes from single-stranded, complementary regions of polynucleotides, and this statement indicates that the invention is different from what is defined in the claim(s) because the current claim set is now drawn to a method of determining the presence of a target nucleic acid

in a sample, which has been construed as encompassing the detection of any nucleic acid in any sample.

Conclusion

28. Rejections and/or objections that appeared in the prior Office action and which were not repeated hereinabove have been withdrawn.

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

30. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

32. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

33. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
23 November 2004